

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

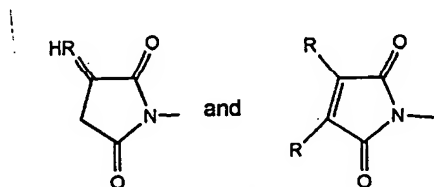
1. (currently amended): A composition comprising a block copolymer having an overall ionic charge and associated with the polymer a biologically active compound having a charge opposite that of the polymer and is characterised in that block copolymer comprises at least one zwitterionic block which has pendant zwitterionic groups and at least one ionic block which comprise ionic groups to confer said overall ionic charge.
2. (currently amended): A composition according to claim 1 in which the biologically active compound is anionic, ~~preferably polyanionic~~.
3. (currently amended): A composition according to claim 2 in which ~~where~~ the active compound is a nucleic acid.
4. (currently amended): A composition according to claim 3 in which the nucleic acid is selected from the group consisting of oligo nucleotides, having 5 to 80 bases, single stranded RNA, single stranded DNA and double stranded DNA, ~~preferably plasmid DNA~~.
5. (original): A composition according to claim 1 in which the biologically active compound is an anionic drug.
6. (currently amended): A composition according to ~~any preceding claim~~ claim 1 in which the biologically active compound and polymer are associated with one another in the form of particles having an average diameter less than 200 μm .

7. (original): A composition according to claim 6 which is an aqueous composition in which the particles are suspended.

8. (currently amended): A composition according to ~~any preceding claim~~claim 1 in which the zwitterionic block is formed from ethylenically unsaturated monomers including a zwitterionic monomer having the general formula



in which Y is an ethylenically unsaturated group selected from the group consisting of $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4-\text{A}^1-$, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{CO}-\text{CR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}-$, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,



A is $-\text{O}-$ or NR^1 ;

A^1 is selected from the group consisting of a bond, $(\text{CH}_2)_l\text{A}^2$ and $(\text{CH}_2)_l\text{SO}_3^-$ in which l is 1 to 12;

A^2 is selected from the group consisting of a bond, $-\text{O}-$, $\text{O}-\text{CO}-$, $\text{CO}-\text{O}$, $\text{CO}-\text{NR}^1-$, $-\text{NR}^1-\text{CO}$, $\text{O}-\text{CO}-\text{NR}^1-$, and $\text{NR}^1-\text{CO}-\text{O}-$;

R is hydrogen or C_{1-4} alkyl;

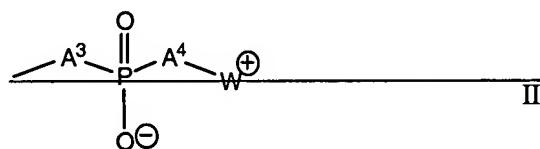
R^1 is hydrogen, C_{1-4} alkyl or BX ;

R^2 is hydrogen or C_{1-4} alkyl;

B is selected from the group consisting of a bond, ~~or~~ a straight and branched alkanediyl groups, alkylene oxaalkylene groups, ~~or~~ and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

X is a zwitterionic group.

9. (currently amended): A composition according to claim 8 in which X is an comprises a cation selected from the group consisting of ammonium, phosphonium, or and sulphonium groups and an anion selected from the group consisting of phosphate or and phosphonate ester zwitterionic group, more preferably a group of the general formula II



in which the moieties A^3 and A^4 , which are the same or different, are O , S , NH or a valence bond, preferably O , and W^+ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is preferably a C_{1-12} -alkanediyl group,

preferably in which W^+ is a group of formula

$\text{W}^+ - \text{N}^+ \text{R}^3_3$, $\text{W}^+ - \text{P}^+ \text{R}^4_3$, $\text{W}^+ - \text{S}^+ \text{R}^4_2$ or $\text{W}^+ - \text{Het}^+$ in which:

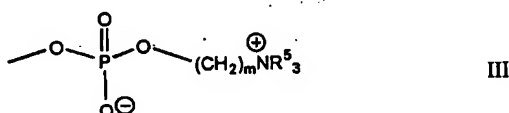
W^+ is alkanediyl of 1 or more, preferably 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted aryl (arylene), alkylene arylene, arylene alkylene, or alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or alkylene cycloalkyl alkylene, which group W^+ optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R^3 are the same or different and each is hydrogen or alkyl of 1 to 4 carbon atoms, preferably methyl, or aryl, such as phenyl, or two of the groups R^3 together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R^3 together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R^3 is substituted by a hydrophilic functional group, and

the groups R^4 are the same or different and each is R^3 or a group OR^3 , where R^3 is as defined above; or

~~Het is an aromatic nitrogen, phosphorus or sulphur, preferably nitrogen, containing ring, for example pyridine groups.~~

10. (currently amended): A composition according to claim 8 in which X has the ~~preferred~~ general formula III



where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4, ~~in which preferably the groups R^5 are the same preferably methyl.~~

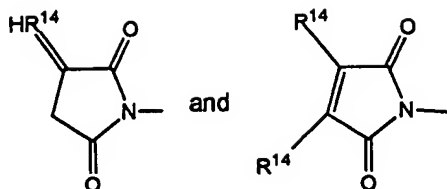
11. (currently amended): A composition according to ~~any of claims 8 to 10~~ claim 8 in which the ethylenic unsaturated group Y is $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, in which R is ~~preferably~~ hydrogen or methyl and A is ~~preferably~~ NH or, ~~more preferably~~, O.

12. (currently amended): A composition according to ~~any of claims 8 to 11~~ claim 8 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.

13. (currently amended): A composition according to ~~any preceding claim~~ claim 1 in which the ionic block is formed of ethylenically unsaturated monomers including an ionic monomer of general formula VI



in which Y^1 is selected from the group consisting of $\text{H}_2\text{C}=\text{CR}^{14}-\text{CO}-\text{A}^8-$, $\text{H}_2\text{C}=\text{CR}^{14}-\text{C}_6\text{H}_4-\text{A}^9-$, $\text{H}_2\text{C}=\text{CR}^{14}-\text{CH}_2\text{A}^{10}$, $\text{R}^{16}\text{O}-\text{CO}-\text{CR}^{14}=\text{CR}^{14}-\text{CO}-\text{O}$, $\text{R}^{14}\text{CH}=\text{CH}-\text{CO}-\text{O}$, $\text{R}^{14}\text{CH}=\text{C}(\text{COOR}^{16})\text{CH}_2-\text{CO}-\text{O}$,



A⁸ is -O- or NR¹⁵;

A⁹ is selected from the group consisting of a bond, (CH₂)_qA¹⁰ and (CH₂)_qSO₃- in which q is 1 to 12;

A¹⁰ is selected from the group consisting of a bond, -O-, O-CO-, CO-O, CO-NR¹⁵-, -NR¹⁵-CO, ~~O-CO-NR¹⁵~~, O-CO-NR¹⁵, and NR¹⁵-CO-O-;

R¹⁴ is hydrogen or C₁₋₄ alkyl;

R¹⁵ is hydrogen, C₁₋₄ alkyl or B¹Q;

R¹⁶ is hydrogen or C₁₋₄ alkyl;

B¹ is selected from the group consisting of a bond, ~~or a straight~~ and branched alkanediyl groups, alkylene oxaalkylene groups, ~~or and~~ alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

Q is an ionic or ionisable moiety.

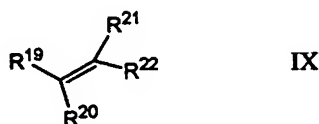
14. (currently amended): A composition according to claim 13 in which Q is selected from groups having the formula -NR¹⁷_p, -PR¹⁷_p and SR¹⁷_r, in which p is 2 or 3, r is 1 or 2, the groups R¹⁷ are the same or different and each is selected from the group consisting of hydrogen, C₁₋₂₄ alkyl and aryl, or two of the groups R¹⁷ together with the heteroatom to which they are attached from a 5 to 7 membered heterocyclic ring or three R¹⁷ groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring, either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R¹⁷ groups may be substituted by amino or hydroxyl ~~groups~~ groups or halogen atoms.

15. (currently amended): A composition according to claim 14 in which Q is $-NR^{17}_2$ where each R^{17} is the same and is C_{1-12} -alkyl, ~~preferably ethyl.~~

16. (currently amended): A composition according to ~~any of claims 13 to 15~~ claim 13 in which B^1 is a C_{2-6} -alkanediyl, ~~preferably $(CH_2)_{2-6}$.~~

17. (currently amended): A composition according to claim 8 ~~and/or claim 13~~ in which the ethylenically unsaturated monomers include comonomer.

18. (currently amended): A composition according to claim 17 in which the comonomer has the general formula IX



in which R^{19} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{23}$ in which R^2 is hydrogen and C_{1-4} alkyl;

R^{20} is selected from the group consisting of hydrogen, halogen and C_{1-4} alkyl;

R^{21} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{23}$ provided that R^{19} and R^{21} are not both $COOR^{23}$; and

R^{22} is selected from the group consisting of a C_{1-10} alkyl, a C_{1-20} alkoxy carbonyl, a mono- or di- $(C_{1-20}$ alkyl) amino carbonyl, a C_{6-20} aryl-~~(including alkaryl)~~ a C_{7-20} aralkyl, a C_{6-20} aryloxy carbonyl, a C_{1-20} -aralkyloxy carbonyl, a C_{6-20} arylamino carbonyl, a C_{7-20} aralkyl-amino, a hydroxyl or a and C_{2-10} acyloxy groups, any of which may have one or more substituents selected from the group consisting of halogen atoms, alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine ~~(including mono and di-alkyl amino and trialkyl ammonium in which the alkyl groups may be substituted)~~, carboxyl, sulphonyl, phosphoryl, phosphino, ~~(including mono and di-alkyl phosphine and tri-alkyl phosphonium)~~, zwitterionic, hydroxyl groups, vinyloxy carbonyl

~~and other vinyl or allyl substituents, and reactive silyl or~~ silyloxy groups, such as trialkoxysilyl groups;

or R²² and R²¹ or R²² and R²⁰ may together form -CONR²⁴CO in which R²⁴ is a C₁₋₂₀ alkyl group.

19. (currently amended): A composition according to ~~any preceding claim~~ claim 1 in which at least one of the blocks has a polydispersity of molecular weight less than 2.0, ~~preferably in the range 1.1 to 1.4.~~

20. (currently amended): A composition according to ~~any preceding claim~~ claim 1 in which the degree of polymerisation of the ionic block is in the range 5 to 2000, ~~preferably 10 to 250,~~ and the degree of polymerisation of the zwitterionic block is in the range 2 to 1000, ~~preferably 5 to 100,~~ and in which the ratio of the degrees of polymerisation ~~(ionic:zwitterionic)~~ of the ionic block to the zwitterionic block is in the range 1:5 to 10:1, ~~preferably 1:1 to 5:1.~~

21. (currently amended): A composition according to ~~any of preceding claim~~ claim 1 in which at least one of the blocks is formed by a living radical polymerisation process; ~~preferably a group or atom transfer polymerisation process.~~

22. (currently amended): A composition according to ~~any preceding claim~~ claim 1 in which the relative amounts of biologically active compound and polymer are in the range 1:5 to 10:1, ~~preferably 1:2 to 5:2~~ based on equivalents of the polymer to active compound charged groups.

23. (currently amended): Process for producing a composition according to claim 1 in which an aqueous dispersion of a block copolymer having an overall ionic charge and comprising at least one zwitterionic block which has pendant zwitterionic groups and at least one zwitterionic block which comprise ionic groups to confer said overall ionic charge, is contacted

with a biologically active compound having a charge opposite that of the block copolymer, to form an aqueous suspension of block copolymer and associated active.

24. (original): Process according to claim 23 in which the average particle size of the suspension is less than 200nm.

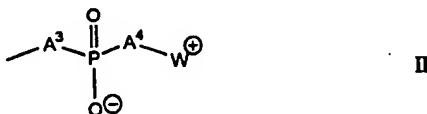
25. (currently amended): Process according to claim 23 ~~or claim 24~~ in which the ratio of equivalents of ionic groups in the block copolymer to ionic groups in the biologically active compound is in the range 10:1 to 1:5, ~~preferably 2:1 to 2:5~~.

26. (currently amended): A process according to ~~any of claims 23 to 25~~ claim 23 in which the biologically active is in solution form in an aqueous vehicle when it is contacted with the block copolymer dispersion.

27. (canceled).

28. (new): A composition according to claim 2 in which the biologically active compound is polyanionic.

29. (new): A composition according to claim 9 in which X has the general formula II



in which the moieties A^3 and A^4 , which are the same or different, are -O-, -S-, -NH- or a valence bond and W^+ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is a C_{1-12} alkanediyl group.

30. (new): A composition according to claim 29 in which W^+ is a group of formula $-W^1-N^+R^3_3$, $-W^1-P^+R^4_3$, $-W^1-S^+R^4_2$ or $-W^1-Het^+$ in which:

W^1 is selected from the group consisting of alkanediyl of 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, and alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or alkylene cycloalkyl alkylene, which group W^1 optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R^3 are the same or different and each is selected from the group consisting of hydrogen, alkyl of 1 to 4 carbon atoms, and aryl or two of the groups R^3 together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or

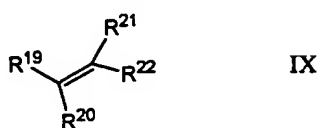
the three groups R^3 together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R^3 is substituted by a hydrophilic functional group, and

the groups R^4 are the same or different and each is R^3 or a group OR^3 , where R^3 is as defined above; and

Het is an aromatic nitrogen-, phosphorus- or sulphur-containing ring.

31. (new): A composition according to claim 13 in which the ethylenically unsaturated monomers include a comonomer.

32. (new): A composition according to claim 31 in which the comonomer has the general formula IX



in which R^{19} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{23}$ in which R^{23} is hydrogen or C_{1-4} alkyl;

R^{20} is selected from the group consisting of hydrogen, halogen and C_{1-4} alkyl;

R^{21} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{23}$ provided that R^{19} and R^{21} are not both $COOR^{23}$; and

R^{22} is selected from the group consisting of C_{1-10} alkyl, a C_{1-20} alkoxy carbonyl, mono- and di-(C_{1-20} alkyl) amino carbonyl, C_{6-20} aryl, C_{7-20} aralkyl, C_{6-20} aryloxy carbonyl, C_{1-20} -aralkyloxy carbonyl, C_{6-20} arylamino carbonyl, C_{7-20} aralkyl-amino, hydroxyl and C_{2-10} acyloxy groups, any of which may have one or more substituents selected from the group consisting of halogen atoms, alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine, carboxyl, sulphonyl, phosphoryl, phosphino, zwitterionic, hydroxyl, vinyloxy carbonyl and reactive silyl and silyloxy groups;

or R^{22} and R^{21} or R^{22} and R^{20} may together form $-CONR^{24}CO$ in which R^{24} is a C_{1-20} alkyl group.

33. (new): A composition according to claim 20 in which the degree of polymerisation of the ionic block is in the range 10 to 250, the degree of polymerisation of the zwitterionic block is in the range 5 to 100 and the ratio of the degrees of polymerisation of the ionic block to the zwitterionic block is in the range 1:1 to 5:1.

34. (new): A composition according to claim 21 in which the living radical polymerisation process is a group or atom transfer polymerisation process.

35. (new): A composition according to claim 22 in which the said relative amounts are in the range 1:2 to 5:2.

36. (new): A process according to claim 23 in which the biologically active compound is anionic.

37. (new): A process according to claim 36 in which the biologically active compound is polyanionic.

38. (new): A process according to claim 36 in which the active compound is a nucleic acid.

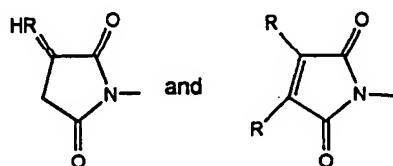
39. (new): A process according to claim 38 in which the nucleic acid is selected from the group consisting of oligo nucleotides, having 5 to 80 bases, single stranded RNA, single stranded DNA and double stranded DNA.

40. (new): A process according to claim 23 in which the zwitterionic block is formed from ethylenically unsaturated monomers including a zwitterionic monomer having the general formula

Y B X

I

in which Y is an ethylenically unsaturated group selected from the group consisting of $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4$ A¹-, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{COCR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}$ -, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,



A is -O- or NR¹;

A¹ is selected from the group consisting of a bond, $(\text{CH}_2)_I\text{A}^2$ and $(\text{CH}_2)_I\text{SO}_3^-$ in which I is 1 to 12;

A² is selected from a bond, -O-, O-CO-, CO-O, CO-NR¹-, -NR¹-CO, O-CO-NR¹- and NR¹-CO-O-;

R is hydrogen or C₁₋₄ alkyl;

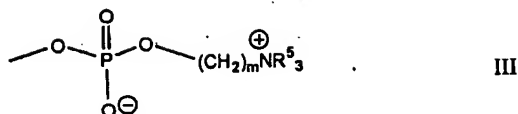
R¹ is hydrogen, C₁₋₄-alkyl or BX;

R² is hydrogen or C₁₋₄ alkyl;

B is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups, and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

X is a zwitterionic group.

41. (new): A process according to claim 40 in which X has the general formula III



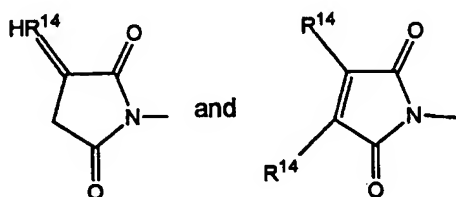
where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4.

42. (new): A process according to claim 40 in which the zwitterionic monomer is 2-methacryloyloxyethyl-2'-trimethylammonium ethyl phosphate inner salt.

43. (new): A process according to claim 23 in which the ionic block is formed of ethylenically unsaturated monomers including an ionic monomer of general formula VI



in which Y^1 is selected from the group consisting of $H_2C=CR^{14}-CO-A^8-$, $H_2C=CR^{14}-C_6H_4-A^9-$, $H_2C=CR^{14}-CH_2A^{10}$, $R^{16}O-CO-CR^{14}=CR^{14}-CO-O$, $R^{14}CH=CH-CO-O-$, $R^{14}CH=C(COOR^{16})CH_2-CO-O-$,



A^8 is $-O-$ or NR^{15} ;

A^9 is selected from the group consisting of a bond, $(CH_2)_qA^{10}$ and $(CH_2)_qSO_3-$ in which q is 1 to 12;

A^{10} is selected from the group consisting of a bond, $-O-$, $O-CO-$, $CO-O$, $CO-NR^{15}-$, $-NR^{15}-CO$, $O-CO-NR^{15}-$ and $NR^{15}-CO-O-$;

R^{14} is hydrogen or C_{1-4} alkyl;

R^{15} is hydrogen, C_{1-4} -alkyl or B^1Q ;

R^{16} is hydrogen or C_{1-4} alkyl;

B^1 is selected from the group consisting of a bond, straight and branched alkanediyl groups, alkylene oxaalkylene groups and alkylene (oligooxalkylene) groups, optionally containing one or more fluorine substituents; and

Q is an ionic or ionisable moiety.

44. (new): A process according to claim 43 in which Q is selected from groups having the formula $-NR^{17}_p$, $-PR^{17}_p$ and SR^{17}_r , in which p is 2 or 3, r is 1 or 2, the groups R^{17} are the same or different and each is selected from the group consisting of hydrogen, C_{1-24} alkyl and aryl, or two of the groups R^{17} together with the heteroatom to which they are attached form a 5 to 7 membered heterocyclic ring or three R^{17} groups together with the heteroatom to which they are attached form a 5 to 7 membered heteroaromatic ring, either of which rings may be fused to another 5 to 7 membered saturated or unsaturated ring, and any of the R^{17} groups may be substituted by amino or hydroxyl groups or halogen atoms.